Evaluation of bone mineral density in thyrotoxicosis

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ABSTRACT

Introduction: This project aimed to study the incidence and profile of bone involvement in thyrotoxicosis patients by dual energy X-ray absorptiometry (DEXA) scan and the effect of treatment on the bone mineral density (BMD).

Methods: A total of 50 young patients with a mean age of 29.4 years, diagnosed to have thyrotoxicosis clinically and proven by thyroid function tests, were included in this prospective three-year study conducted at the Madras Medical College and Government General Hospital in Chennai, India. Patients were enrolled if they had bone pain or had elevation of serum alkaline phosphatase. All these patients had a baseline BMD measurement by DEXA scans in the region of the lumbar vertebrae before treatment and the T-score was computed. All other secondary causes of low BMD, like primary hyperparathyroidism, long-term steroid intake, vitamin D deficiency, was ruled out. After definitive management of hyperthyroidism by anti-thyroid drugs and surgery, all the patients with bone involvement had a repeat DEXA scan after one year and the T-score was computed.

Results: Out of 50 patients, 46 had bone involvement (92 percent). Based on the World Health Organisation classification, 16 (32 percent) had osteopenia and 30 patients (60 percent) had osteoporosis. After control of thyrotoxicosis, the mean bone mass increased from 0.729 g/sq cm to 0.773 g/sq cm, a statistically significant increase of 0.044 g/sq cm (p-value is less than 0.001) after one year, compared to age- and sex-matched controls. The mean percentage of the bone mass compared to the peak BMD increased from 70.2 percent to 74.2 percent after treatment, an increase of four percent (p-value is less than 0.001). The mean percentage of the bone mass compared to the age-matched BMD increased from 71.2 percent to 75.2 percent after treatment, an increase of four percent (p-value is less than 0.001), all of which were statistically significant.

Conclusion: Metabolic bone disease should be looked for in all thyrotoxic patients, especially patients complaining of bone pain and those with elevated bone enzymes. DEXA scans offer a convenient, reliable and non-invasive modality for diagnosis and monitoring therapy.

Keywords: bone mineral density, dual energy x-ray absorptiometry, metabolic bone disease, osteoporosis, thyrotoxicosis

INTRODUCTION

Diseases of the thyroid gland are a common occurrence in India. Thyrotoxicosis, a clinical syndrome characterised by manifestations of excess thyroid hormone, is one of the commonly-recognised conditions of the thyroid gland. Thyrotoxicosis causes acceleration of bone remodelling and even though it is one of the known risk factors for osteoporosis, the metabolic effects of thyroxine on bone is a little-discussed subject. There are largely limited studies in India as to whether these changes are reversible. In this study, we note the incidence and profile of bone involvement in thyrotoxicosis patients by dual energy x-ray absorptiometry (DEXA) scan and the effect of treatment on the bone mineral density (BMD) after control of thyrotoxicosis.

METHODS

A total of 50 young patients with a mean age of 29.4 years, diagnosed to have thyrotoxicosis clinically and proven by thyroid function tests, were included in this prospective three-year study conducted in...
were treated with subtotal thyroidectomy and six (12%) were treated with radioactive iodine ablation (RAI). RAI was chosen because four patients refused surgery and one patient developed agranulocytosis with anti-thyroid drugs. All patients were monitored with thyroid function tests monthly to detect hypothyroidism. Thyroid function tests returned to normal after a mean period of 1.2 ± 0.4 months after treatment. Thyroid function tests and DEXA scans were again repeated after 12 months.

RESULTS

Of the 50 patients with thyrotoxicosis with bone pain or elevated alkaline phosphatase, 30 (60%) complained of bone pain and 40 (80%) had elevated alkaline phosphatase (Table I). Of 50 patients, 46 (92%) had bone involvement and four (8%) had a normal BMD, irrespective of bone pain, and elevated serum alkaline phosphatase of bony origin. Of these 46 patients, 16 (32%) had osteopenia and 30 (60%) had osteoporosis, according to the WHO classification (Table II). Patients were evaluated by repeat DEXA scan after 12 months of treatment. The mean lumbar bone mass increased from 0.729 g/cm$^2$ to 0.773 g/cm$^2$, an increase of 0.044 g/cm$^2$ (p<0.001).

The mean percentage of the bone mass compared to the peak BMD increased from 70.2% to 74.2% after treatment, an increase of 4% (p<0.001). The mean percentage of the bone mass compared to the age-matched BMD increased from 71.2% to 75.2% after treatment, an increase of 4% (p<0.001), all of which were statistically significant. The mean serum alkaline phosphatase decreased from 2.18 ± 0.2 microKat/L to 1.25 ± 0.1 microKat/L (p<0.001), which was also statistically significant after treatment (Table III). The mean free thyroxine after 12 months done at the time of DEXA scan was 1.8 ± 0.3 ng/dL.

One more significant observation of our study was that the detrimental effects of thyroxine on bone were more pronounced in women. They had a mean BMD of 0.700 g/cm$^2$, compared to men who had a mean BMD of 0.763 g/cm$^2$. Women also showed a lesser increment in their bone mass (mean increase 0.027 g/cm$^2$) compared to men (mean increase 0.065 g/cm$^2$). This finding implies that women with thyroxine-induced bone disease need a more aggressive treatment programme than men to correct it.

DISCUSSION

Our study shows that patients with active thyrotoxicosis have reduced lumbar spine BMD measurements that increased after therapy. These data suggest that thyrotoxic bone loss may therefore
be reversible. The first case of thyrotoxic osteopathy was reported in 1891 by von Recklinghausen(12). Several later cross-sectional studies have shown reduced bone mineral measurements in thyrotoxic patients(1-7). Fraser et al recorded a 7% reduction in forearm cortical bone using γ-densitometry(2), and Auwerx and Bouillon et al recorded a 13% reduction in lumbar spine bone mineral using dual-photon absorptiometry(7). The benefits of anti-thyroid therapy on the skeleton in thyrotoxicosis have recently been addressed because of the worldwide interest in the prevention of osteoporosis.

Longitudinal studies done on patients successfully treated for thyrotoxicosis have produced conflicting data but on the whole, suggest that thyrotoxic bone loss is potentially reversible(3,5,6,11). Studies reported by Bayley et al(3) using neutron-activated analysis, by Toh et al(6) using single-photon absorptiometry, and by Krolner et al(5) using dual-photon absorptiometry, have all shown increases in bone mineral varying from 3.7% to 12.9%. We have taken a cross-section of patients with thyrotoxicosis suffering from bone pain or with elevated alkaline phosphatase. Particular attention was paid to the measurement of bone mineral density by DEXA scan. The identification of osteopenia or osteoporosis secondary to thyrotoxicosis alters the management. Our study in these 50 thyrotoxic patients amply proves the fact that metabolic bone disease is a common occurrence in these patients.

The clinician should suspect the presence of bone disease in a thyrotoxic patient (especially if long-standing) who complains of bone pain and has elevated serum alkaline phosphatase. Once suspected, BMD is measured using DEXA scan and it is one of the best ways of diagnosing and documenting the extent of bone changes in hyperthyroidism.

Another advantage of DEXA scan is to monitor individuals’ response to therapy. Our study has demonstrated that more than 90% of patients demonstrate some changes in BMD if patients are chosen based on symptoms of bone pain or with elevated serum alkaline phosphatase, as defined by DEXA scan. With the use of investigations like serum PTH, 25-hydroxy-vitamin D, we excluded any significant cause of decreased bone mass. Decrease in bone mass could be caused by genetic factors, decreased weight, cigarette smoking or alcoholism. It would seem unlikely that this is the cause of decreased bone mass as the patients were age- and sex-matched and smokers and alcoholics were excluded from the study. It would also seem unlikely in the event that there was an increase in the bone mass after correction of the thyrotoxic state.

In conclusion, metabolic bone disease should be looked for in all thyrotoxic patients, especially patients complaining of bone pain and those with

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<th>Table I. Clinical details of the 50 patients studied.</th>
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<td>Age (years)</td>
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<td>Sex</td>
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<td>Disease duration (years)</td>
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<th>Table II. Bone mineral density (BMD) in thyrotoxicosis patients.</th>
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<td>BMD</td>
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<td>Normal (T-score &gt; -1)</td>
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<tr>
<td>Osteopenia (T-score = -1 to -2.5)</td>
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<td>Osteoporosis (T-score &lt; -2.5)</td>
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<th>Table III. Serum biochemistry and BMD measurements in patients with thyrotoxicosis before and after 12 months of anti-thyroid therapy.</th>
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<td>Variable (baseline value)</td>
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<tr>
<td>Alkaline phosphatase (1.14 ± 0.1 microKat/L)</td>
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<td>Lumbar bone mass (1.1 ± 0.04 g/cm²)</td>
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<td>Percentage of BMD compared to peak BMD (95 ± 2%)</td>
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<td>Percentage of BMD compared to age-matched control (95 ± 2%)</td>
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Baseline data are shown as mean ± standard deviation. p-value <0.001 compared to controls in all variables.
elevated bone enzymes. DEXA scans offer a convenient, reliable and non-invasive modality for diagnosis and monitoring therapy. Women are more susceptible to the bone depleting effects of thyroxine\(^{(19)}\); hence, they require a more aggressive treatment programme than men. Thyrotoxic bone loss may be reversible. Successful treatment of the thyrotoxic state with anti-thyroid therapy may result not only in a return to normal of bone turnover but also in an improvement in bone mineralisation. We found that lumbar spine bone mineral, which is composed predominantly of cancellous bone, showed the greatest increase.

REFERENCES